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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/358,755 | 07/22/1999 | HIROSHI KAWABATA | 008708-D7024 | 1939 |

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EXAMINER

MURPHY, JOSEPH F

| ART UNIT | PAPER NUMBER |
|----------|--------------|
|----------|--------------|

1646

DATE MAILED: 04/08/2002

22

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/358,755

Applicant(s)

KAWABATA ET AL.

Examiner

Joseph F Murphy

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 February 2002.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 12-18, 20-23, 43-58 and 60-70 is/are pending in the application.
- 4a) Of the above claim(s) 12-18 and 20-23 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 43-57, 60-62 is/are allowed.
- 6) ☒ Claim(s) 58 and 63-70 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

Formal Matters

Claims 72-79 were cancelled in Paper No. 21, 2/1/2002. Claims 12-18, 20-23, 43-58, 60-70 are pending. Claims 12-18, 20-23 stand withdrawn from consideration pursuant to 37 CFR 1.142(b).

Response to Amendment

The rejections of claims 72-79 have been rendered moot by cancellation of the claims.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 63-70 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleotide sequence consisting of SEQ ID NO: 2 and SEQ ID NO: 3, does not reasonably provide enablement for a nucleotide sequence consisting of substantially the same nucleotide sequence of SEQ ID NO: 2 and SEQ ID NO: 3. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 63 is overly broad in the recitation of "substantially the same nucleotide sequence" since no guidance is provided as to which of the myriad of polynucleotide species encompassed by the claim will encode proteins which retain the characteristics of TfR. In the specification (page 8, lines 15), Applicants disclose that variants of the polynucleotide have sufficient homology to the reference polynucleotide such that it will hybridize under moderate conditions,

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without disclosing any actual or prophetic examples on expected performance parameters of any of the possible encoded muteins of TfR. However, it is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, Mikayama et al. (1993) teaches that the human glycosylation-inhibiting factor (GIF) protein differs from human migration inhibitory factor (MIF) by a single amino acid residue (page 10056, Figure 1). Yet, despite the fact that these proteins are 90% identical at the amino acid level, GIF is unable to carry out the function of MIF, and MIF does not exhibit GIF bioactivity (page 10059, second column, third paragraph). It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

There is insufficient guidance provided in the specification as to how one of ordinary skill in the art would generate a nucleic acid sequence encoding TfR other than those exemplified in the specification. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors considered to be relevant in the instant case are set forth below:

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(1) the breadth of the claims - The claims included in the instant rejection are drawn to a nucleotide sequence consisting of substantially the same nucleotide sequence of SEQ ID NO: 2 and SEQ ID NO: 3.

(2) the nature of the invention - The instant invention is a nucleic acid encoding a protein.

(3) the state of the prior art - The Mikayama and Voet references demonstrate that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the encoded protein's function.

(5) the level of predictability in the art - The Mikayama and Voet references demonstrate the unpredictability of the protein art.

(6) the amount of direction provided by the inventor - Applicant has only taught SEQ ID NO: 2 and SEQ ID NO: 3, and not any nucleic acids substantially the same as SEQ ID NO: 2 or 3 that encode TfR polypeptides.

(7) the existence of working examples - Working examples are provided only for the protein encoded by SEQ ID NO: 2 and 3.

(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. Since the claims encompass nucleic acids which are substantially the same as SEQ ID NO: 2 and 3, and no guidance is provided to place a structural limitation on the claims, it would require the skilled artisan to determine which are the encoded amino acid residues which are necessary for TfR function to make and use the claimed invention.

Given the breadth of claims 63-70 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in

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the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 58, 63-70 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "substantially" in claim 63 is a relative term which renders the claim indefinite. The term "substantially" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention. Claims 64-70 are rejected insofar as they depend on the recitation of the term "substantially".

Claim 58 is vague and indefinite because there is unclear if the mRNA is complementary to the whole length of SEQ ID NO: 2 or 3, or merely to a portion of it.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely

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exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 63 recites the broad recitation "substantially the same" and also recites "consisting of" which is which is the narrower statement of the range/limitation.

Conclusion

Claims 58, 63-70 are rejected.

Claims 43-57, 60-62 are allowable.

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Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245.

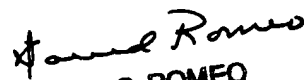
The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.



Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
April 1, 2002


DAVID S. ROMEO
PRIMARY EXAMINER